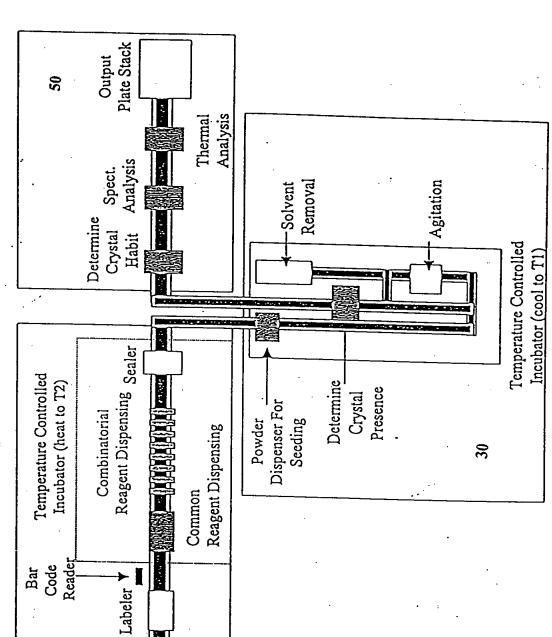


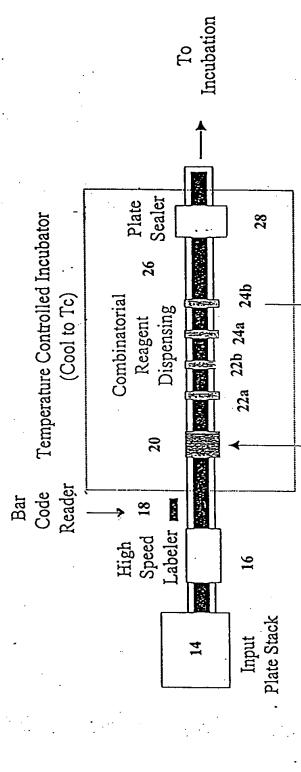
Combinatorial Mixing of Crystallization Components

In-Depth Characterization of Lead Candidates



Input Plate Stack

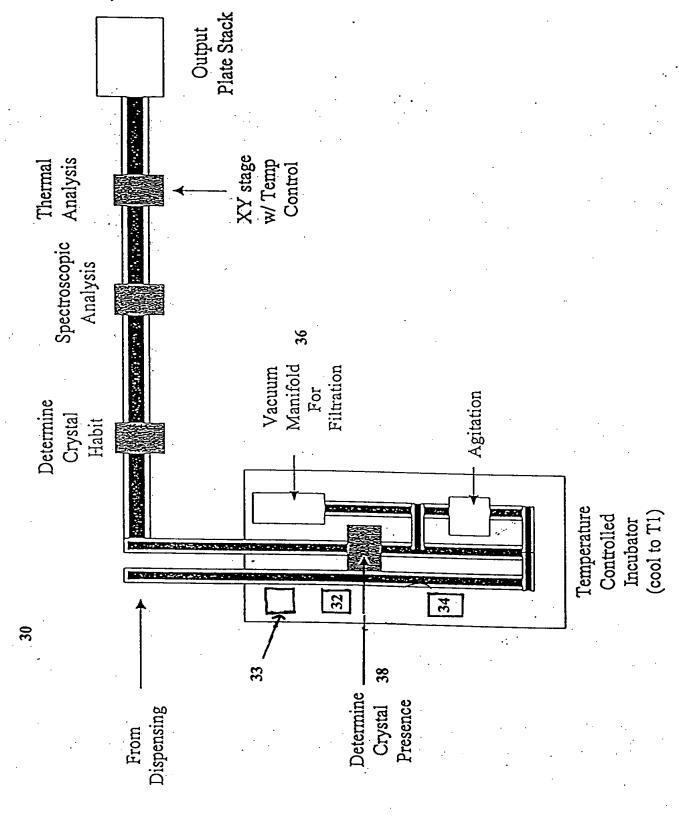
Incubation and Dynamic Scanning of Precipitants



Nanoliter Dispensing

Common Reagent Dispensing





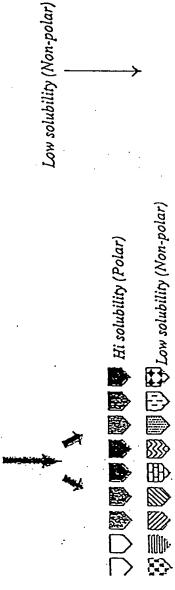
Isothermic crystallization

Generation of stock saturated solutions using

II. Distribute stock solutions/generate mixtur

Hi solubility (Polar)

A. Add excess compound to each stock colution



100% 80% 60% 40% 10% 5%

00000000

00000000 00000000 00000000

000000000

00000000 00000000 00000000 00000000

B. Throughly mix, filter solutions to remove any undisolved material

II. Monitor precipitation (optical density)

III. Examine crystallinity by birefringence

IV. Test crystal forms by XRPD

IV. Different crytals tested by DSC and TG

l emperature-mediated crystallization

I. Generation of stock saturated solutions using

A. Add excess compound to each stock colution at various temps 80°C, 60°C, 40°C, 20°C, 10°C



B. Throughouly mix, filter solutions to remove any undisolved material. Maintain original temperature

II. Temperature ramp downs

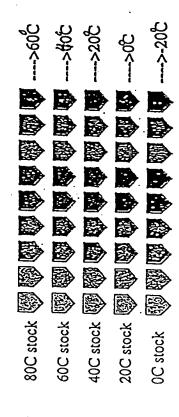


FIG. 3C

Evaporative crystallization

I. Generation of stock saturated solutions using

II. Controlled pressure ramp down (temperature)

A. Add excess compound to each stock solution



2 atm

1 atm

0.1 atm

0.01 atm

B. Thoroughly mix, filter solutions to remove any

un-dissolved material. Maintain original temperature

Raman IntensityWavenumber

